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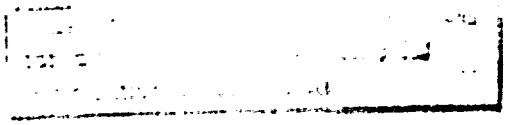

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[illegible] OF THE STABILITY OF CELLS TO THE DIPHTHERIA TOXIN UNDER THE INFLUENCE OF A LATENT VIRAL INFECTION

[Following is the translation of an article by A. A. Zabrov, Laboratory of Aerobic Infections, Leningrad Research Institute of Vaccines and Sera, and Department of Virology, Institute of Experimental Medicine of the Academy of Medical Sciences of the USSR, Leningrad, published in the Russian-language periodical Tsitologiya (Cytology) 8:767--769, 1966. It was submitted on 22 Jul 1966.]

The phenomenon of interference has been known for a long time in the practice of virology. It amounts to the fact that cells which are infected with virus turn out to be non-susceptible to repeated infection. It turned out that infected cells developed a particular protein substance which possessed an antiviral activity. This substance was named interferon, (Isaacs and Lindenmann, 1957). It has been established that interferon does not act on the virus but on the cell. Under the influence of interferon conditions are created in the cell in which the virus cannot develop its infectious activity. This protective effect is non-specific: interferon, developed under the influence of one virus, imparts to the cells a resistance to the most diverse viruses. And what is more, interferon and its connected resistance to viruses may appear following the influence on non-infected cells not only of viruses, but also of several other agents: nucleic acids (Rotem et al., 1963), bacteria (Youngner and Stineberg, 1964), endotoxins (Stineberg and Youngner, 1964), etc. Data have been obtained that interferon-like substances, forming during the influence of non-viral agents on a cell, already exist in it, being found in an inactive state under the influence of repressors or included in the composition of compounds which are broken down under the influence of the stated stimuli (Wagner, 1965).

The non-specificity of the protective effect of interferon for separate viruses, the possibility of its previous existence in cells, and the manifestation of activity under the influence of substances of a non-viral nature point to the thought that the antiviral action of interferon is only a partial case of a wider phenomenon of change in the sensitivity of cells taking place with its participation. It is true that for checking this assumption it is necessary to determine if there is an increase in the resistance of cells in the presence of interferon to the effects of any agents besides the viruses. In the present work the results

are given from an investigation of the sensitivity of cells of a monolayer culture from tissues of 10-day old chick embryos, infected with the virus of louping ill, to the cytopathogenic effect of diphtheria toxin. The louping ill virus during its multiplication in the stated culture does not cause any apparent cytopathogenic changes. During examination under the microscope the infected cells are no different from the control. Against a background of a latently proceeding viral infection the development of interferon takes place, in connection with which attempts of repeated infection of such a culture with another virus turn out to be unsuccessful.

3-day cultures were infected with the louping ill virus on a calculation of 10^4 tissue infectious doses per 1 ml of medium 199. The control test tubes contained 1 ml each of medium 199 which did not contain the virus. After a 2-day incubation at a temperature of 37°C the titer of interferon in the liquid phase of the infected cultures in various tests comprised from 1:32 to 1:64. These cultures were resistant to the action of an indicator virus of vesicular stomatitis which was administered in a quantity of 10^5 tissue cytopathogenic doses per 1 ml. Parallel with resistance to virus a test was made of the resistance of these cultures to toxin. For this 2 days after infection with virus of louping ill successive dilutions of toxin were introduced into the cultures. At the same time control non-infected cultures were inoculated with toxin. Results were considered based on the findings of microscopic examination. With a sufficient dose of toxin distinct cytopathogenic changes were visible in 2--3 days after its administration (granularity of protoplasm, rounding of cells, disruption of integrity of the cell layer).

As can be seen from the table, the cells which were preliminarily infected with louping ill virus turned out to be more resistant to the cytopathogenic effect of diphtheria toxin. In all cases the concentration of toxin necessary for their impairment was greater than in the control. Using the terminology which is accepted in the practice of virology, it can be said in these cases that "interference" of the louping ill virus with diphtheria toxin took place. Data on the effect of other bacterial toxins will be presented in another paper.

Summary

Cells from tissue cultures of chick embryos, infected with the louping ill virus, displayed increased resistance not only to the cytopathogenic action of indicator virus, but also to diphtheria toxin. This testifies to the fact that resistance to the virus is only a partial manifestation of the condition of increased resistance which develops in a cell during the process of development of interferon.

influence of latent infection, caused by the louping ill virus, on the sensitivity of cells of tissue cultures of chick embryo to the cytopathogenic action of diphtheria toxin

(a) Вариант опыта	Величины максимального разведения токсина, при котором еще наблюдается цитопатогенный эффект, полученные в 5 разных опытах (b)				
	1	2	3	4	5
(c) Культура, зараженная вирусом	7000	6500	3500	1000	500
(d) Незараженная культура (контроль)	1200	8000	7000	3000	1500

Key: (a) Variant of experiment; (b) Values of maximum dilution of toxin, obtained in 5 different tests, at which a cytopathogenic effect is still observed; (c) Culture infected with virus; (d) Non-infected culture (control).

Literature

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